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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/766,873	01/19/2001	Hongsheng Su	104385.132	9057
23483	7590	03/23/2004	EXAMINER	
HALE AND DORR, LLP 60 STATE STREET BOSTON, MA 02109			HUTSON, RICHARD G	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/766,873	SU ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 February 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,5-22,26 and 30-34 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,5-22,26 and 30-34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/3/2004 has been entered.

Applicants cancellation of claims 2-4, and 35, amendment of claims 1, 9-11, 21 and 26, in the paper of 1/19/2004, has been entered and thus acknowledged. Applicants' arguments filed on 1/19/2004, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Claims 1, 5-22, 26, 30-34 are still at issue and are present for examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 (10-12 dependent on) is indefinite in that it is confusing in the recitation "... **further** comprising a selectable marker..." Specifically it is unclear as to applicants intended meaning of the word "further" in the context of the claim. Is it applicants intent to further limit the selectable marker of claim 1, in which case the word "further" is unnecessary, or is it applicants intent that the host cell of claim 9 comprises an additional selectable marker, in addition to the one described in claim 1? For the purpose of advancing prosecution the claim is interpreted as per the first option, in which case it is suggested that applicants delete the word "further" or explain why such is not necessary.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5-22, 26 and 30-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection is stated in the previous office action as applied to claims 1-22, 13-21, 26 and 30-35. In response to this rejection applicants have cancelled claims 2-4 and 35 and amended claims 1, 10, 21, 26 and traverse the rejection as it applies to the newly amended claims.

Applicants traverse on the basis that applicants claims fully comply with the guidelines for written description and that applicants were in possession of the claimed

invention, a new *Flavobacterium heparinum* host system for expressing heparinase enzymes or selectable markers using expression vectors, as supported in applicants examples 1, 2 and 4 of applicants specification.

Applicants traversal is not found persuasive as applicants disclosure of the *F. heparinum* host cells transformed with the expression vectors, pIBXF1 and pIBXF2, does not describe a *F. heparinum* host cell transformed with any expression vector. Applicants disclosure of a mere two examples of a plasmid which may be used to transform *F. heparinum* does not adequately describe the genus of "any expression vector".

Given the lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1, 5-22, 26 and 30-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a *Flavobacterium heparinum* transformed with pIBFX1 and pIBFX2, does not reasonably provide enablement for a *Flavobacterium heparinum* transformed with any expression vector. The specification does not enable any person skilled in the art to which it pertains, or with which it is most

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nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection is stated in the previous office action as applied to claims 1-22, 13-21, 26 and 30-35. In response to this rejection applicants have cancelled claims 2-4 and 35 and amended claims 1, 10, 21, 26 and traverse the rejection as it applies to the newly amended claims.

Applicants traverse this rejection on the basis that applicants specification and examples teach and demonstrate to one of skill in the art how to make the expression vectors of the present invention and how to obtain expression in *F. heparinum*.

Applicants are reminded that the applicants specification and examples teach and demonstrate to one of skill in the art how to make the expression vectors pIBFX1 and pIBFX2 and how to obtain expression in *F. heparinum* using these vectors, not any and all possible expression vectors. As most if not all "expression vectors" cause expression of at least some protein/gene that could reasonably considered a "selectable marker", applicants amendment still reads on a extremely broad genus of *F. heparinum* host cells transformed a practically any expression vector.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any *Flavobacterium heparinum* transformed with any expression vector. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired

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biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 5-11, 13-21, 26 and 30-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmerman et al. (WO 96/01894, January 25, 1996) and McBride et al. (Applied and Environmental Microbiology, Vol. 62, No. 8, pages 3017-3022, August 1996).

The original rejection is stated in the previous office action, paper of 12/13/2002, and maintained in the office action of 6/3/2003, as applied to claims 1-11, 13-21, 26 and 30-35. In response to this rejection applicants have cancelled claims 2-4 and 35 and amended claims 1, 10, 21, 26 and traverse the rejection as it applies to the newly amended claims.

Applicants submit that the above claims are not rendered obvious by the combination of Zimmerman and McBride, as the use of expression vectors for expression of heparinase I, heparinase II, heparinase III, or a selectable marker in a *F. heparium* host is not taught or suggested by Zimmerman or McBride alone or in

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combination. Applicants submit that applicants are teaching the expression of homologous or heterologous gene sequences encoding at least one of heparinase I, heparinase II, heparinase III, or a selectable marker in a *F. heparinum* in an expression system using expression vectors, not the tn4351 transposon DNA.

Applicants argument is not found persuasive because applicants are reminded that the original rejection stated that while the original rejection stated "one of ordinary skill in the art at the time of filing would have been motivated to express the genes encoding the *Flavobacterium heparinum* enzymes, chondroitinase AC and chondroitinase B, in *Flavobacterium heparinum* under the control of an overexpression promoter in a suitable expression system, such as the tn4351 transposon DNA", the motivation was not specifically to the expression in the tn4351 transposon DNA. The reference to the success of the tn4351 transposon DNA of McBride et al. is used mainly as a measure of the expectation of success, showing that such an expectation of success was high.

Applicants statement supporting applicants above argument, referring to applicants own publication, Su et al. (Microbiology Vol. 147, pp 581-589, 2001, especially page 585, col. 2, first full paragraph) in which the authors state that "previous attempts to use transposons into *F. heparinum* failed", is acknowledged. Such a statement appears to more appropriately support an argument against the reasonable expectation of success that was previously and above suggested as obvious over Zimmerman and McBride et al. An argument against the expectation of success based on the results of McBride et al. in light of applicants above statements in the Su et al.

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publication is not found persuasive. The mere statement that "applicants" failed to successfully transfer broad-host-range plasmids and transposons into *F. heparinum* is insufficient in voiding the previously stated reasonable expectation of success. Further applicants attention is directed to claim 8, which further limits claim 1, specifically limiting the claim such that the recombinant DNA is integrated through any of bacteriophage integration, transposition of a transposon and transposition on an insertion sequence element.

Thus claims 1, 5-11, 13-21, 26 and 30-34 are obvious by Zimmerman et al. and McBride et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read 'Richard G. Hutson', with a long horizontal line extending to the right.

Richard G Hutson, Ph.D.
Primary Examiner
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Rgh
3/19/2004